PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
International application No. PCT/US2004/039781	International filing date *(day/month/year)* 24.11.2004	Priority date *(day/month/year)* 26.11.2003
International Patent Classification (IPC) or national classification and IPC INV. C12Q1/68		
Applicant ADVANDX, INC. et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 10 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in celectronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24.06.2005	04.08.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Bellmann, A Telephone No. +31 70 340-

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/039781

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-31 as originally filed

   Sequence listings part of the description, Pages

   1-3 received on 01.08.2005 with letter of 29.07.2005

   Claims, Numbers

   1-59 as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-3 (partially), 5-8, 10-13(completely), 14-59(partially)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-3 (partially), 5-8, 10-13, (completely), 14-59(partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-3, 14-59 (partially), 4 and 9 (completely) .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	14-24,26-32,34-50,52-59
	No:	Claims	1-4,9,25,33,51
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-4,9,14-59
Industrial applicability (IA)	Yes:	Claims	1-4,9,14-59
	No:	Claims	-

2. Citations and explanations (Rule 70.7):

   see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

   and / or

2. Non-written disclosures (Rule 70.9)

   see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☒ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

The following documents are referred to in this communication:

D1: US-B1-6 380 370 (DOUCETTE-STAMM LYNN A ET AL) 30 April 2002 (2002-04-30)
D2: EP-A-1 096 024 (FACULTES UNIVERSITAIRES NOTRE-DAME DE LA PAIX) 2 May 2001 (2001-05-02)
D3: WO 99/01572 A (ID BIOMEDICAL CORPORATION; BEKKAOUI, FAOUZI; CLONEY, LYNN, P) 14 January 1999 (1999-01-14)
D4: WO 00/66788 A (GEN-PROBE INCORPORATED; HOGAN, JAMES, J; GORDON, PATRICIA) 9 November 2000 (2000-11-09)
D5: WO 03/052128 A (HVIDOVRE HOSPITAL; WESTH, HENRIK; LISBY, GORM) 26 June 2003 (2003-06-26)
D6: EP-A-0 957 175 (ACADEMISCH ZIEKENHUIS GRONINGEN; RIJKSUNIVERSITEIT TE GRONINGEN) 17 November 1999 (1999-11-17)

1. Re Item IV
Lack of unity of invention

1. The common concept linking together the inventions are PNA probes specific for one or more *Staphylococcus* species other than *S. aureus*. PNA probes for the specific detection of *Staphylococcus* species other than *S. aureus*, e.g. *S. epidermidis* are however well-known in the prior art; cf. for example D1 (cf. cl.1, col.8, par.1, col.11, par.1), D2 (cf. cl.1,9, par.32 and 41), D3 (cf. cl.1,11,12,15, p.9, par.2), D4 (cf. cl.1,14, p.20, par.1), D5 (cf. cl.71, 84, p.32, par.2) or D6 (cf. cl.17,24, par.21 and 60). Therefore, the subject-matter is not linked within a single general inventive concept.

2. In view of the prior art, the problem of the underlying application can be defined as the provision of alternative PNA probes specific for one or more *Staphylococcus* species. Invention 1 is a PNA probe comprising a nucleobase sequence suitable for the analysis of *Staphylococcus epidermidis*. Invention 2 to 8 are a PNA probe comprising a nucleobase sequence suitable for the analysis

of *Staphylococcus hominis*, *S. haemolyticus*, *S.lugdunensis*, *S.saprophyticus*, *S. warneri*, *S.sciuri* and *S.schleiferi* respectively.

3. Due to the fact that there is no single general inventive concept, that the PNA probes represent independent solutions and that no special technical features in the sense of Rule 13.1 PCT can be identified, the subject-matter claimed does not fulfil the requirements of unity set forth in Rule 13.1 PCT. Consequently, there is lack of unity and the 8 solutions given, which represent different inventions not belonging to a common inventive concept are formulated as the different subjects on the communication pursuant to Article 17(3) PCT.

Invention 1: claims 1-3, 14-59 (partially), 4 and 9 (completely)

PNA probe comprising a nucleobase sequence suitable for the analysis of *S. epidermidis*, probe sets and kits comprising said probe and methods for analysing *S. epidermidis*.

Invention 2: claims 1-3, 14-59 (partially), 5 and 10 (completely)

PNA probe comprising a nucleobase sequence suitable for the analysis of *S. hominis*, probe sets and kits comprising said probe and methods for analysing *S. hominis*.

Invention 3: claims 1-3, 14-59 (partially), 6 and 11 (completely)

PNA probe comprising a nucleobase sequence suitable for the analysis of *S. haemolyticus*, probe sets and kits comprising said probe and methods for analysing *S. haemolyticus*.

Invention 4: claims 1-3, 14-59 (partially), 7 and 12 (completely)

PNA probe comprising a nucleobase sequence suitable for the analysis of *S. lugdunensis*, probe sets and kits comprising said probe and methods for analysing *S. lugdunensis*.

Invention 5: claims 1-3, 14-59 (partially), 8 and 13 (completely)

PNA probe comprising a nucleobase sequence suitable for the analysis of *S. saprophyticus*, probe sets and kits comprising said probe and methods for analysing *S. saprophyticus*.

Invention 6: claims 1-3,14,15,25-59 (all partially)

PNA probe comprising a nucleobase sequence, wherein at least a portion of the probe is at least 86% identical to the nucleobase sequence or complement of SEQ ID No.4 suitable for the analysis of *S. warneri*, probe sets and kits comprising said probe and methods for analysing *S. warneri* using said probe.

Invention 7: claims 1-3,14,15,25-59 (all partially)

PNA probe comprising a nucleobase sequence, wherein at least a portion of the probe is at least 86% identical to the nucleobase sequence or complement of SEQ ID No.9 suitable for the analysis of *S. sciuri*, probe sets and kits comprising said probe and methods for analysing *S. sciuri* using said probe.

Invention 8: claims 1-3,14,15,25-59 (all partially)

PNA probe comprising a nucleobase sequence, wherein at least a portion of the probe is at least 86% identical to the nucleobase sequence or complement of SEQ ID No.10 or 11 suitable for the analysis of *S. schleiferi*, probe sets and kits comprising said probe and methods for analysing *S. schleiferi* using said probe.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability WITH REGARDS TO THE FIRST INVENTION; citations and explanations supporting such statement

2. **NOVELTY** (Article 33(2) PCT)

1. INDEPENDENT CLAIM 1

A PNA probe comprising a nucleobase sequence suitable for the analysis of *Staphylococcus epidermidis* is disclosed in D1 (cf. cl.1, col.8, par.1, col.11, par.1), D2 (cf. cl.1,9, par.32 and 41), D3 (cf. cl.1,11,12,15, p.9, par.2), D4 (cf. cl.1,14, p.20, par.1), D5 (cf. cl.71, 84, p.32, par.2) and D6 (cf. cl.1,6,17,24, par.21 and 60).
Therefore, the subject-matter of independent claim 1 is not novel over D1 to D6 (Article 33(2) PCT).

2. INDEPENDENT CLAIM 25

A PNA probe set comprising one or more PNA probes suitable for the analysis of *Staphylococcus epidermidis* and at least one PNA probe for the analysis of S.aureus is disclosed in D2 (cf. par.32 and 41), D4 (cf. cl.1, 14 and p.20, par.1) and D6 (cf. cl.17,24 to 26).
Therefore, the subject-matter of independent claim 25 is not novel over D2, D4 and D6 (Article 33(2) PCT).

3. INDEPENDENT CLAIM 33

A method for the analysis of *Staphylococcus epidermidis* in a sample, comprising:
a) contacting at least one of PNA probe to the sample,
b) hybridizing the PNA probe to a target sequence of *Staphylococcus epidermidis*; and
c) detecting the hybridization, wherein the detection of hybridization is indicative of the presence, identity and/or amount of *Staphylococcus epidermidis,* is disclosed in D2 (cf. cl.1,9,32 and par.41), D3 (cf. cl.1,11,12 and p.9, par.2), D4 (cf. cl.30 and p.20, par.1), D5 (cf. cl.1,12,13 and p.32, par.2) and D6 (cf. cl.1,17).
Therefore, the subject-matter of independent claim 33 is not novel over D2 to D6 (Article 33(2) PCT).

4. INDEPENDENT CLAIM 51

A kit suitable for performing an assay for analysis of *Staphylococcus epidermidis*, wherein said kit comprises: a) a PNA probe suitable for analysis of *Staphylococcus epidermidis* and b) other reagents or compositions necessary to perform the assay, is disclosed in D2 (cf. par.32 and 41), D3 (cf. cl.12,16 and p.9, par.2), D4 (cf. cl.40 and

p.20, par.1), D5 (cf. cl.71,84 and p.32, par.2) and D6 (cf. cl.17, 24 to 26 and par.21). Therefore, the subject-matter of independent claim 51 is not novel over D2 to D6 (Article 33(2) PCT).

3. **INVENTIVE STEP** (Article 33(3) PCT)

1. Dependent claims 2 to 4,9, 14 to 24, 26 to 32, 34 to 50 and 52 to 59 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, as all of the additional features fall within the scope of routine laboratory practise.

Re Item VI
Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 2004/053105	24.06.2004	12.12.2003	12.12.2002
WO 2004/029299	08.04.2004	23.09.2003	24.09.2002